REMARKS

STATUS OF THE CLAIMS

Claims 1-5, 12, 16, 21 and 22 were pending in this application. Claims 16 and 22 have been amended. Following entry of the amendments claims 1-5, 12, 16, 21 and 22 will be pending and at issue.

SUPPORT FOR AMENDMENTS TO THE CLAIMS

Claims 16 and 22 have been amended to delete the term "with an effective proximity" and to include the term "wherein the cleavable linkage is susceptible to cleavage when in proximity to the cleavage-inducing moiety" to more clearly define Applicant's invention. Support for the term can be found throughout the specification as filed, e.g., page 28, lines 23-25, and page 29, line 22 to page 30, line 16.

The amendments to the claims therefore add no new matter and entry is respectfully requested.

REJECTIONS UNDER 35 U.S.C. § 112, SECOND PARAGRAPH

Claims 1-5, 12, 16, and 21-22 were rejected under 35 U.S.C. § 112, second paragraph as allegedly indefinite because the results of the assay were said not to be correlated back to the preamble of the method objectives.

The applicants traverse the rejection. The claims recite that the differences in the amounts from the patient sample and the reference sample are correlated to the disease status of the patient. The specification and the Examples in the specification teach how to correlate the differences with the disease status of the patient. Thus, Example 1 shows that the dimerization of PI3K to Her-3 to give the PI3K/Her-3 complex increases in breast cancer cell lines as the concentration of HRG is increased, thereby showing that the severity of cancer correlates with PI3K/Her-3 complex. Thus, in light of the teachings of the specification, one of skill in the art would know how to determine the disease status of the patient based on the relative amounts of the complex. If a skilled artisan would have understood the inventor to be in possession of the

claimed invention at the time of filing, even if every nuance of the claim is not explicitly described in the specification, then the requirement for an adequate written description is met. The Examiner is respectfully requested to withdraw the rejection.

Claims 16 and 22 were rejected under 35 U.S.C. § 112, second paragraph as allegedly indefinite because of the phrase "having a cleavage-inducing moiety with an effective proximity." The applicants have amended the claims to recite that the cleavable linkage is susceptible to cleavage when in proximity to the cleavage-inducing moiety. The Examiner is respectfully requested to withdraw the rejection.

REJECTIONS UNDER 35 U.S.C. § 112, FIRST PARAGRAPH (ENABLEMENT)

Claims 3-5, 12, 16, and 21-22 were rejected under 35 U.S.C. § 112, first paragraph, as allegedly containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. The Examiner stated that BAD/14-3-3 complex is not a validated disease marker, and the specification was said not to provide sufficient guidance to indicate a correlation between the detection of the BAD/14-3-3 complex and any disease.

The applicants traverse the rejection. In Example 3, the applicants simultaneously measure BAD/14-3-3 and BAD/Bcl-2 complexes in serum-starved breast cancer cell line culture (MCF-7), and the results illustrated in Figure 9. The applicants define BAD as a human protein capable of forming a stable complex with a human 14-3-3 protein and capable of forming a stable complex with a human Bcl-2 protein. Bcl-2 is a well known biomarker for breast cancer. The results presented in Example 3 show that BAD/14-3-3 complex correlates with at least breast cancer. The claims are thus enabled. The Examiner is respectfully requested to withdraw this rejection.

REJECTIONS UNDER 35 U.S.C. § 102

Claims 1-2 are rejected under 35 U.S.C. § 102(b) as allegedly being unpatentable over Wildi *et al.* (2001) Gut **49:** 409-417. Applicant traverses this ground of rejection.

In order for a reference to anticipate an invention, the reference must teach each and every element of the claimed invention. The claims recite measuring one or more intracellular complexes. Wildi does not disclose that Activin A is an intracellular complex. Accordingly, the reference does not teach each and every element of the claimed invention and cannot anticipate the claimed invention. Withdrawal of this rejection is requested.

CONCLUSION

Withdrawal of the pending rejections and reconsideration of the claims are respectfully requested, and a notice of allowance is earnestly solicited. If the Examiner has any questions concerning this Response, the Examiner is invited to telephone Applicant's representative at (650) 335-7818.

Respectfully submitted,
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